The Mitral Valve: A Brief History

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The left atrioventricular valve acquired its "mitral" designation through a description by the great renaissance anatomist Andreas Vesalius. In his seminal text De Humani Corporis Fabrica Libri Septum (first edition:1543), he wrote the following. "At the root of the circle of the venous artery (the left atrium), a membranous circle [valvar atrio-ventricularis sinistra] originates from the substance of the heart (the atrioventricular junction) and goes inward into the space of the left ventricle, when it descends a little way into the space of the ventricle it splits into two membranous processes resembling in shape those of the right ventricular membranes being however of only two rather than three on the right side. They are greater in strength than those in the right ventricle. Because the membranous circle of the venous artery (left atrium) is split into only two membranes you would not be wrong in comparing them to a Bishop's Mitre if you compare the part encircling the head to the membranous circle and its processes to the front and the back points of the Mitre" [1].

Vesalius described the function of these membranes of the heart as bodies that are present to prevent regurgitation of material (sanguis). His description is fully recognisable in modern parlance. Outwith the now correct nomenclature, that of the aortic and mural leaflets, Vesalius describes the two leaflets as facing the right and the left sides of the left ventricle. He correctly describes the arching distribution of cordal insertions leaving the underside of the leaflets and inserting into the muscle of the left ventricle. He described how the cords are stabilised by fleshy projections from the ventricular wall (musculus papillares anteriores and posteriores), which we call the antero-superior and infero-lateral papillary muscles. He contrasts his description and comparison to an up-turned Bishop's Mitre to that of Galen, who described the leaflets as being like arrowheads projecting downwards into the ventricular cavity [2]. Thus, as elsewhere in his text, Vesalius reveals a deep knowledge of prior anatomical writings, especially those of the great natural philosophers,

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Hippocrates (460–375 BCE), Aristotle (385–323 BCE), Erasistratus (304–250 BCE), and Galen (129–c.200 AD). Interestingly, there is no mention of the work of that other great renaissance man, Leonardo da Vinci. Thirty years earlier he had extensively written and illustrated his studies on the structure and function of the heart and the valves of the heart. This ground-breaking work, although recognised as important by the few who saw it, was confined to the pages of personal notes never published, underscoring the importance of publishing work for peer review and discussion.

The first known descriptions of the heart begin with an Egyptian papyrus from about 3,000 BCE in which there is a description of the heart and great vessels. The ancient Egyptian understanding of the heart was very much based on the interconnection of mysticism, religion, and spirituality of the human form. Its central importance in the balance of the mind and body is manifest in the assessment of a life by comparing the weight of the feather of Maat with the heart of the deceased, which was laden with the burdens of their lifestyle and moral failures. Maat is the concept of universal balance and harmony, personified in the goddess of that name. It is thus clear that the heart was more than an anatomical structure.

A canon of medicine from around 2,600 BCE ascribed to the legendary Chinese Emperor Huang Ti, recognised that the heart and pulse regulate the blood, which according to this manuscript flows in a continuous circle and never stops. The Greek anatomist and royal physician to Selenicus, Nicator of Syria, founded the school of anatomy in Alexandria with Heroditus. He described the valves of the heart [3]. He also concluded that the heart was not the centre of sensation but was a pump.

Aristotle made mention of the valves of the heart in his books de Respiratione and de partibus Animalium 3, referenced by William Harvey in his masterpiece “de Motu Cordis.” Aristotle called them nerves, with little further comment. Hippocrates, in contrast, wrote as follows “The hidden membranes and fibres spread throughout the chambers like cobwebs especially around the orifices. There are filaments implanted into the walls of the chambers as well. The author believes these to be guy ropes and stays of the heart as well as the foundation of the arteries.” These ultra-modern comments resonate with our modern understanding of the importance of the mitral valvar complex in supporting left ventricular function.

Much of the work of these academic giants has been passed down to us through the work of Avicenna. Abu Ali Sina or Ibn Sina was a Persian polymath. He is regarded as one of the most important and influential physicians, astronomers, and thinkers of the Islamic Golden age. Many of his writings have survived and revealed the heavy influence of Hippocrates. His “Canon of Medicine” is regarded as the founding text of medieval and early modern medicine. Without his extensive discourses on Hippocrates and Galen much of the work of those giants may never have been recognised as they are today.

The Renaissance anatomist Alessandro Benedetti, born in Parma in 1450, physician of Verona and Padua, and surgeon to the Venetian army, described the valves as uni-directional gates. He called them “valvulae,” from the Latin “valva,” a leaf of a folding door. He also began to distinguish the heart as a capacitance pump receiving blood, rather than contributing blood on the basis of the uni-directional control of the flow of the valves. He recognised the importance of the strength of the mitral valve, which he described as the strongest of all of the heart valves. He was responsible for the construction of the first-ever anatomy theatre in Padua, where he carried out his instructional dissections.

Sandwiched between these early renaissance anatomists and Andreas Vesalius, as already emphasised, is the unpublished and largely undiscovered work of the Florentine polymath Leonardo da Vinci. Living from1452 until 1519 and a self-educated natural philosopher, Leonardo set about a very detailed comparative anatomical study of the heart begun in Milan, continued at the family home of his apprentice and long-time travelling companion Francesco Melzi, and completed during his move to Rome in the employment of the Pope. Leonardo spent a year in the Melzi family home, a villa overlooking the river Adda just nineteen miles from Milan. There he was able to pursue his many interests in geology, hydrology, and anatomical dissection. In the absence of human material on which to work, Leonardo invested his efforts in animal dissection, extending his understanding of comparative anatomy. This investment of energy into animal dissection reveals his insistence that all natural forms are diagrams of the forces acting upon them, which was an Aristotelian mantra. On this basis, he argued that physiological function could be deduced from form, whatever the setting. The chapter in this book on the comparative anatomy of the mitral valve (The Atrioventricular valve in the animal kingdom, Bjarke Jensen) reveals the appropriateness of comparisons across species in modern times. Thus the heart, the body's pump, would reveal its secrets through an understanding of hydrology, architecture, and structural form in a way that can be transposed to other settings.

In March of 1513, Giovanni de Medici was elected Pope. He became Pope Leo X; He was the son of Lorenzo "the magnificent" de Medici, the Florentine ruler who had patronised Leonardo whilst in Florence, and recommended him to the Sforza court in Milan, perhaps helping him to escape the hubris of two court appearances for homosexuality. This latter move to Rome allowed Leonardo to recommence his dissection on human cadavers, an activity that it is suggested caused his removal from the employ of Giovanni following an occupational dispute based on the jealousy of a German mirror maker, with whom Leonardo was sharing quarters in the Villa Belvedere within the Vatican. He was returning to a fraternity very familiar to him in the company of Bramante, Michelangelo, and Raphael; not all of them happy relationships. Comparisons of his output whilst in the employ of the Pope with those of his younger competitors became unfavourable in the eyes of his employer. It is during this time that his anatomical studies became very modern, indeed considered "post-modern" at that time. He had moved beyond descriptive anatomy to applied anatomy or as we would term it today, physiological thought.

Leonardo's study of anatomy had endured through much of his life, with the first evidence appearing in his drawing of the fluid systems of the body probably done around 1482 (RL 12597).[1] In this drawing, the heart is depicted in Galenic form as

[1] RL refers to Royal Library catalogue numbering of the manuscript pages held in the possession of the British Royal Family in the Library at Windsor.

a two-chambered structure. A note to the side of the drawing states “Cut through the middle of the heart, liver and lung and the kidneys so that you can represent the vascular tree in its entirety.” This statement of intent came to fruition three decades later with Leonardo’s in-depth study of the internal organs. In these later studies, his approach to understanding the body moved definitively from anatomical structure to how form informed function. The centrepiece of this work was an extensive study of the heart. Virtually all of the drawings from these studies reveal the anatomy of the Ox heart. Whilst Leonardo’s seminal work on the Aortic valve is well known, his important observations on the mitral valve are less recognised. His drawings of the mitral and tricuspid valves reveal his exceptional ability to look, see, and understand the structures under examination. This, coupled with his unique ability as a draughtsman, has left us with some of the most remarkable drawings that impart functional knowledge as well as structural information. Innovation was Leonardo’s middle name. The techniques that he described to allow appropriate viewing of the working heart are yet another example of his genius, and his ability to apply lateral thought. By injecting the hearts with hot wax, and waiting for it to set, and the heart to seize in rigour mortis, he was able to demonstrate the form of this three-dimensional structure as in working life. Thus, he was able to visualise the cordal array beneath the valve as if it was under tension (Fig. 1.1: RL 19119 recto). His drawings of this are truly ground-breaking.

This chapter is not sufficient to discuss Leonardo’s work on the heart in its entirety along with its internal anatomy and physiology, but a fuller description can be found in “The Heart of Leonardo” by this author [4]. In the course of this work, Leonardo correctly described the anatomical structure of the mitral valve and its component parts. His drawings of the ventricular aspect of the valve reveal the arching cordal insertions spreading out to distribute the forces applied to the valve; their insertion into the papillary muscles, shown as extensions of the trabeculated myocardium and their arcading nature into the three principle types, primary secondary and tertiary cords[2,3] (Fig. 1.2). He spent considerable efforts describing the nature of the necessary surfaces of coaptation of the leading edges of the leaflets (see Fig. 1.2). He even indicated measurement of this height; a factor we know is critical to normal valvar function.[4] His engineering sense allowed him to think about the interaction of valve and ventricle. There is a tiny sketch of ropes and pulleys in the middle of a summary page of drawings of the Ox heart indicating his acknowledgement of the interplay of forces between valve and ventricle, the so-called atrioventricular loop, which is vital in maintaining normal ventricular function[5] (Fig. 1.3a, b). He also studied extensively the tricuspid valve and went so far as to describe making a paper

[2] RL 19078 (detail).

[3] RL 19080 recto.

[4] RL 19080 recto & RL 19074 recto.

[5] RL 19074 verso.

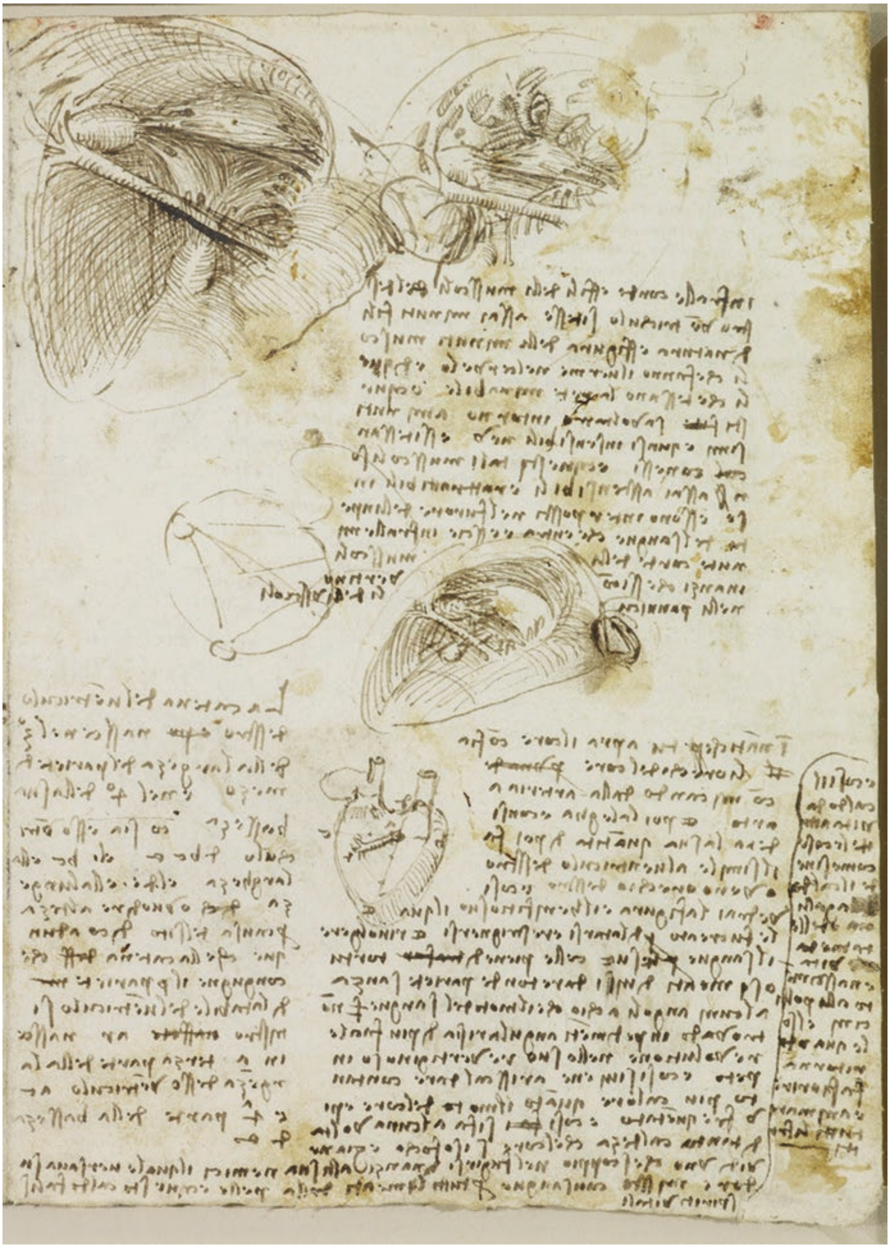

Fig. 1.1 RL 19119 recto. The right ventricle and the Tricuspid valve with the moderator band after distension with hot wax. (Lent by Her Majesty The Queen. Royal collection © Her Majesty Queen Elizabeth II)

Fig. 1.2 RL 19080 recto. Detailed drawings of the Mitral valve by Leonardo visualising the cordal arrays, the mitral valve complex and coaptation of the leaflets as well as the relationship between the aortic and mitral valves. (Lent by Her Majesty The Queen. Royal collection © Her Majesty Queen Elizabeth II)

model to demonstrate leaflet movement (Fig. 1.3c).[6] In describing the function of the cords in preventing eversion of the leaflets allowing mitral regurgitation, he invoked the metaphor of the sails on a sailing boat.[7] As the ropes (Cords) from the Capstan (Papillary muscles) prevent the sail (the leaflets) from being blown inside out, so the Cords support the Mitral leaflets preventing regurgitation.

These observations were not published and thus are not considered in the wider canon of anatomical literature. Of course, with practical applications of this level of knowledge being half a millennium away, it is difficult to know how it might have been applied. We should also remember that Leonardo was seen as something as an upstart in the Academic community of the time as a result of his lacking a classical education. This reflected his artistic training, which was seen as a lowly profession

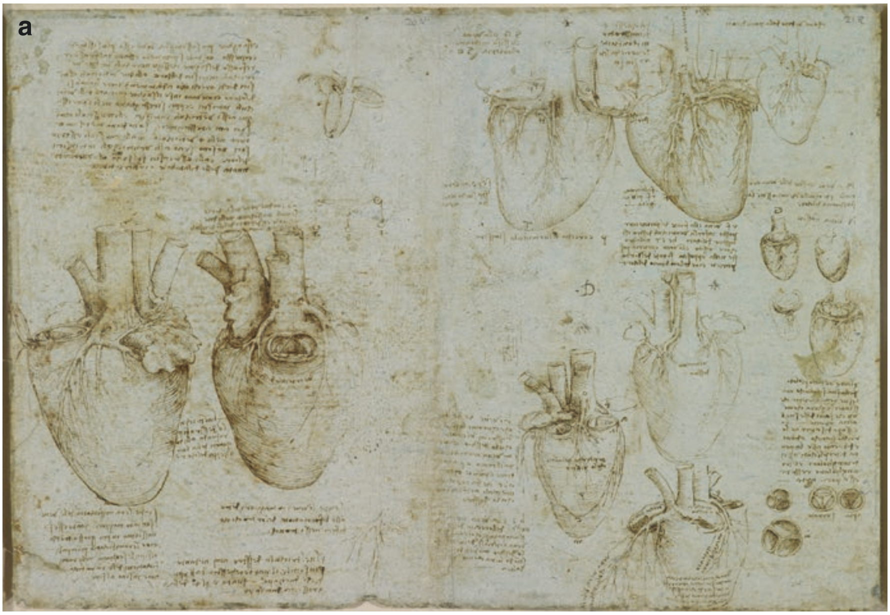

Fig. 1.3 (**a**) RL 19074 verso. (Lent by Her Majesty The Queen. Royal collection © Her Majesty Queen Elizabeth II). (**b**) Detail of RL 19074 verso. A geometrical sketch to illustrate the forces acting on the leaflets and cords of the Mitral valve. (Lent by Her Majesty The Queen. Royal collection © Her Majesty Queen Elizabeth II). (**c**) RL 19704 recto. Detailed analysis of the Tricuspid valve. This includes a description of making a model of the valve for teaching purposes. (Lent by Her Majesty The Queen. Royal collection © Her Majesty Queen Elizabeth II)

[6] RL 19116 verso.

[7] Madrid manuscript II f. 121 verso.

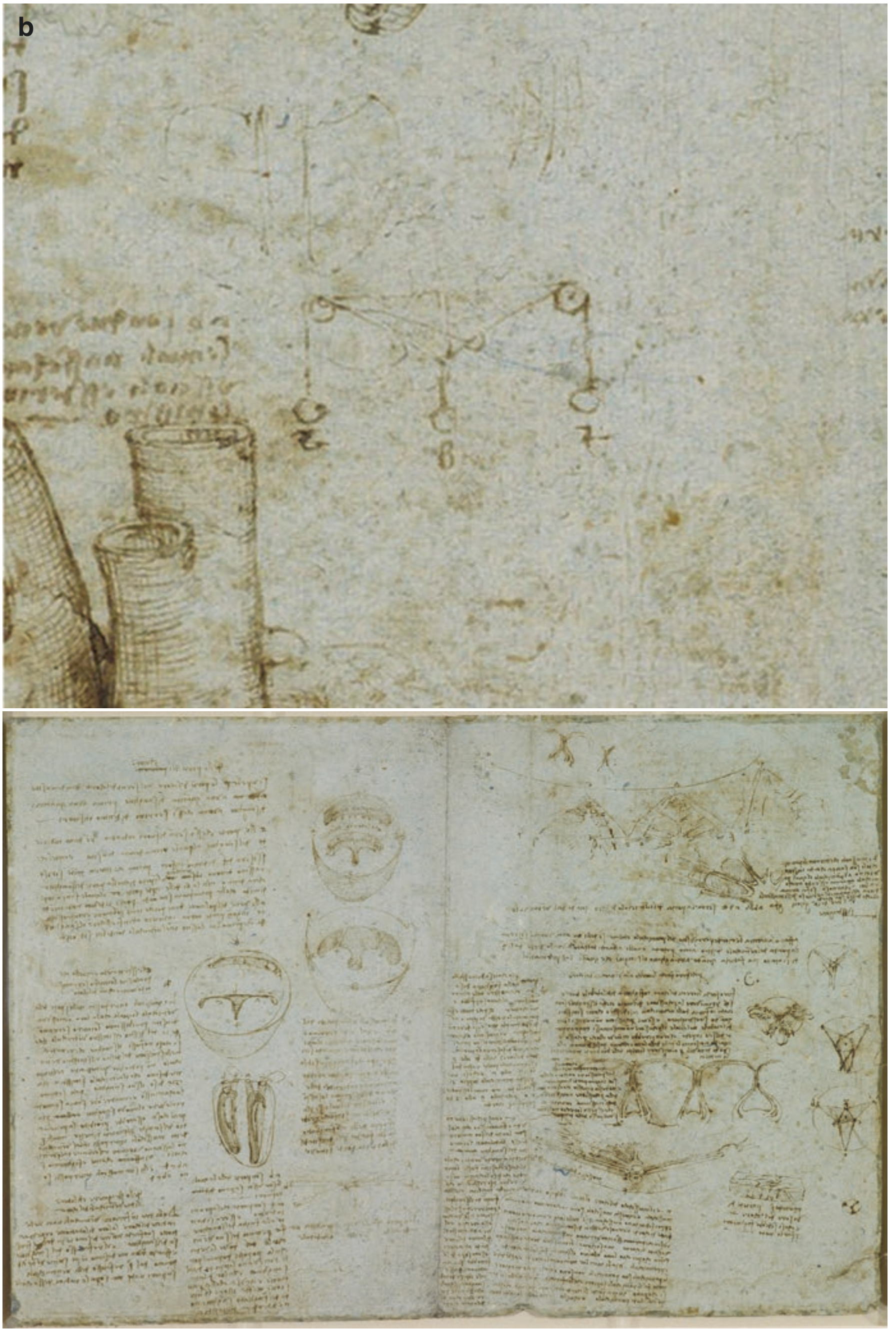

Fig. 1.3 (continued)

at the time. We can but marvel at his genius today, as the relevance of his observations unfurls with our own developing knowledge.

As mentioned earlier, William Harvey, who lived from 1578 through 1657, introduced his discussion of the atrioventricular valves by alluding to the fact that Aristotle had considered the cords and papillary muscles to be nerves in the heart. Aristotle was aware that muscles could not contract without the presence of nerves, and abstracted this thought to the heart. Harvey described the presence of "tendons and fleshy twigs with very many fibrous connections within the ventricle, of which some apart are stretched with divers motions and are partly hidden in furrows with deep ditches about them in the walls and mediastinum, and they are like a kind of little muscles which are superadded to the heart as auxiliaries for the further expulsion of the blood, that like the diligent and artificial provision of tackling in a ship they might help the heart contracting itself everyway and might squeeze more blood more fully and forcibly out of the ventricles.[8]

Harvey discussed the comparative anatomy of the atrioventricular valves, and detailed the necessity of the left ventricle having the thickest muscle by the nature of the work that it has to do delivering blood to the whole of the body rather than just to the lungs. He described the mitral valve as having the appearance of a "mitre" but without referencing the use of this name to the work of Vesalius. Whether it is an independent observation of his, or an absence of attribution, we cannot know. The omnipresence of religion at those times, however, may have been the stimulus for both men to use this term. His colourful terminology for the right atrioventricular valve describes it as having three forked portals, with the left-sided valve as having only two, and hence mimicking the Bishop's Mitre. This, he suggested, allows tighter closure than the right valve. He describes the cords of the valve being tendons that reach far out, even to the conus of the ventricle, through its middle "that they may be most exactly shut." Harvey had significant difficulty in getting his theory of the circulation accepted and support sprung from a perhaps unexpected quarter. René Déscartes, the great French philosopher, mathematician, and scientist, whilst opposing Harvey's ideas of ventricular function, recognised in a mechanistic discussion that the presence of the atrioventricular valves could allow only unidirectional flow, supporting the premise of the continuous circulation that was still being rejected by many important physicians and scientists of the time. In a letter to Beeverwijck he wrote, "the valves prevent the blood from backing up "in agreement with the laws of mechanics.".[9] Déscartes dispute with Harvey was over the cause of the movement of the heart. Descartes maintained that cardiac movement was caused by the flow of the blood, whereas Harvey maintained the Aristotelian position, namely that the heart was a muscle, and hence the progenitor of movement. This position was then reinforced by the work of Richard Lower, of whom more later,

[8]The Anatomical Excercises of Dr. William Harvey. De Motu Cordis 1628. The first English text of 1653, newly edited by Geoffrey Keynes. Chapter XVII. P. 107. Issued by the Lustar press on the quadricentennial of the birth of Dr William Harvey. Limited to 1578 copies.

[9]Letter to Beverwijk, July 5, 1643, AT IV 5.

who demonstrated that the heart continued to beat after removal from the body of an animal.

Harvey then conceded that his own investigations of the internal structure of the heart were incomplete, but that he intended to return to it when he had the time. It is interesting, especially in the context of this book, that he recognised the importance of understanding both the embryology of the heart and its comparative anatomy. In this, he compared himself with the approach of Aristotle, who studied the developing chicken's embryo and the initial pulsation of the heart visible in the foetal stage.[10]

A further interesting observation from Harvey's writing in de Motu Cordis is the fact that he used boiling of the heart to unravel the aggregated cardiomyocytes, commenting that all anatomists from Galen on had used this technique. His observations on the mitral and tricuspid valves, however, were scant, and simply define their presence as proof of maintenance of the forward and onward flow of the blood. His use of the presence of valves as underscoring the truth of the circulation is focussed on the work of Acquapendente (Hieronymous Fabricius from Acquapendente and, Italy 1533–1619) and Realdo Colombo (1516–1559) on the presence and function of valves within the peripheral veins and the valve at the entrance of the inferior caval vein to the right atrium.

Enter Dr. Richard Lower, a physician and scientist who was trained in part by the great Thomas Willis, of the circle of Willis. Lower had a stellar career. He worked extensively on the potential for transfusion of blood, and on the structure and function of the heart. In his latter years, he acted as royal physician to King Charles II in his final illness. In 1669, he published his own magnum opus "Tractus de Corde" [5]. In this publication Lower fulfilled Harvey's promised, but never delivered, further description of the structure and movement of the heart. He discussed the function of the papillary muscles and valvar leaflets in a modern fashion [6]. An example of his gift with words is as follows describing the tricuspid valve, "Thus when the apex of the heart is drawn nearer to the base in each systole the papillae also move upwards and slacken their fibres (Cords) to very loose reins; the membranes to which they are attached follow suit and hanging loose are driven upwards like bellying sails by the expulsion of blood at each systole of the heart. In consequence of this they close the opening of the heart so exactly that not even the smallest drop can flow back into the auricle but is expelled into the lungs where no such hindrance bars its way. But while the apex is drawn nearer the base at each Systole of the Heart and the papillae slacken their fibres in diastole the apex goes back again and draws down with it the papillae and their fibres. Hence the membranes are likewise withdrawn and uncover at once the entrance into the heart, opening the doors, as it were, to the inflow of blood from the auricle [7]." These words evoke those of Leonardo 150 years earlier. As did Leonardo, he went on to suggest that the presence of the papillary muscles prevented the leaflets from reaching the walls of the ventricle so that they were able to return to the closed position more easily rather than be trapped against the walls by the flowing blood. This ingenious proposition is not considered today, but is probably relevant to the normal valvar function. Lower described

[10] Ibid., Chapter XVII, page 113.

passing a pipette into the ventricle through the apex and injecting water under pressure to demonstrate the closure of the valve. He also described the injection of water across the valve to demonstrate full and complete closure, as we use in surgery today when testing the repaired valve during the operation. Lower then emphasised the greater strength of the valvar apparatus on the left side of the heart to accommodate the much higher left ventricular systolic pressure.

Three great eighteenth-century anatomists, William Cheselden, (The Anatomy of the Humane Body 1713), John Hunter, 1728–1793 (A Treatise on the Blood Inflammation and Gun-shot wounds 1794), and his brother William Hunter 1718–1783 (Lecture notes on Anatomy), each wrote about the valves of the heart, but each of their descriptions was limited to the simple anatomical statement of parts and the physiological function of preventing regurgitation of ventricular blood in systole.

By the middle of the nineteenth century Henry Gray had produced his Magnus opus "Anatomy Descriptive and Surgical', known ever since simply as "Gray's anatomy." The first edition reproduces the simple descriptions of the mitral valve to be found in the works of the previous century. This has continued until recent times, with some minor additions regarding valvar and commissural closure.

It was not until meaningful surgical procedures become available, and the truly intimate relationship between the valve and ventricular function became appreciated, that the anatomical descriptions of the mitral valve really took on a functional aspect. In 1964, Dr. Walton Lillehei, a major cardiac surgical pioneer based in Minneapolis, recognised that, when the mitral valve was simply cut away from the ventricle, disrupting all of the support of the tension apparatus provided by the left ventricle, patients suffered progressive left ventricular failure no matter how successful the replacement valvar surgery had been. This resulted in the death within 5 years of surgery of around half of the patients undergoing surgery. In his seminal paper on this subject, Lillehei wrote the following, "Early in our series with this valve, we experienced a post-operative mortality significantly higher than anticipated when compared with that of patients having reconstructive procedures in similar functional status. The mortality in this early experience with the ball valve was mainly due to "low cardiac output" syndrome associated with apparent excellent prosthesis function [8]."

The functional anatomy of the valve began to be seriously appreciated around this time, with sophisticated experiments on the movements of the valve [9]. Strikingly, in the absence of replacement prostheses, the early attempts at surgery on the valve had been through reconstruction. It was in stark contrast to these early promising results that the detrimental effect of complete excision of the valve became apparent. It was not until another three decades had past, however, that through the excellent work of surgeons such as Dwight McGoon at the Mayo clinic and Alain Carpentier at l'hopital Broussais in Paris the true superiority of mitral valvar preservation and reconstruction became apparent.

One of the earliest descriptions of the mitral valve as an interconnected complex was by Perloff ad Roberts [10]. In their words, "The Mitral apparatus is a complex, finely coordinated mechanism that can be deranged by a multiplicity of acquired and congenital disorders and requires for its competence the functional integrity of the anatomic elements working in delicate concert. These anatomic elements are: 1. Posterior left atrial wall, 2. The annulus, 3. Leaflets, 4. Chordae tendineae, 5. Papillary muscles, and 6. Left ventricular wall."

And so, it is today that we really have come to appreciate the sophisticated physiology, interplaying with its complex anatomy that the mitral valve has really come of age. Truly understanding it and its central role in normal cardiac function has become an exciting specialism all of its own. It may be thought of as the lynchpin of efficient ventricular function. Just as the mitral crown sits on top of the head of the Church, so does its biological counterpart sit as the prince of all the internal organs.[11]

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[11] "The heart is as it were a Prince in the Commonwealth, in whose person is the first and highest government everywhere; from which as from the original and foundation, all power in the animal is derived, and doth depend." The Anatomical exercises of Dr. William Harvey de Motu Cordis 1628. From the first English text 1653. Translation by Geoffrey Keynes.